DETAILED ACTION

The office action mailed 9/27/11 is vacated and replaced with the action herein. Applicants have requested a more thorough reassessment of the claim rejections. In this vein, the rejection under 35 SUC 101 has been withdrawn and based upon this a new rejection under 35 USC 103 instated.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/12/11 has been entered.

Claims 1-3 and 5-23 are pending. Claim 20 is an improper multiple dependent claims that do not refer to the claims in the alternative, e.g. claim 1 and 14 are both required in one alternative. Hence, claim 20 has been withdrawn from examination. See MPEP § 608.01(n).

Claim Objections

Claims 1, 3, 6, 8, 11, 14, 15, 17-19, 21 and 23 are objected to because of the following informalities: **These are objections maintained from the office action mailed 9/14/11.**

The recommendation made in the rejection mailed 9/14/10 stands wherein it is proper to recite in claim 1, line 4, --a coding sequences for a site-specific integrase --.

When referring to previous limitations, the word "said" is used when the reference uses the terms as previously recited in exact terms. In this case, "said" is used improperly in claim 3 when referring to "said genes encoding the structural proteins".

Claim 8 formatting is improper in that the groups are recited as if the promoters are all of the promoters from 16S, 23S rRNA or all of those form polymerases, transcription, replication or translation factors. It would be remedial to recite, --a promoter of the ribosomal subunit 16s, a promoter of ribosomal subunit 23s, a polymerase promoter, a transcription promoter, a replication promoter or a translation factor promoter--.

The comma following "a reporter protein" in claim 11 is grammatically incorrect.

The recitation in claim 14, "is E. coli or sulfolobus" is grammatically incorrect. As well, E. coli should be italicized. The claim should recite, --is *E. coli* or a *sulfolobus* cell.

In claim 17 the phrase "(poly)peptide" is inconsistent with previous recitations. **Applicants argue that the phrase is not vague nor indefinite. However, the recitation "said (poly)peptide is not supported by the claim. The claim previously recites polypeptide whereas (poly)peptide implies that the structure can be a peptide or a polypeptide. This is not supported by the claim.**

In claim 18 the article "a" is required in line 2 prior to SSV1 and SSV2 and the article "the' prior to SSV2 in step (a) and prior to SSV1 and SSV2 in step (b).

These are new objections.

Claim 1 requires a comma prior to "the site specific" in line 7.

Claim 6 recites that the vector has a promoter for expression of the gene of interest, whereas the vector of claim 1 already comprises a promoter for expression of the gene of interest.

In claim 19, "a gene of interest" is improper and should be –the gene of interest--. When referring to limitations previously recited, it is proper to use the article "the".

Claim 21 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 1. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Both claims are drawn to the same essential protein from sulfolobus.

In claim 23 it is not clear how sequences 3' of the gene of interest can be an N-terminal extension. The specification actually states that the vector comprises 3' to the translation initiation site of the promoter additional nucleic acid sequences that are the N-terminal extension.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 6, 8-15, 17 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Stedman et al Genetics **152:** 1397–1405 (August 1999). **This rejection is maintained for reasons of record in the office action mailed 2/3/10 and restated below.**

Stedman et al teach a vector that comprises the SSV1 genome and hence inherently comprises each of an ori, genes encoding the structural proteins and site-specific integrase from SSV1 each operably linked to expression control sequences. As well, the vector comprises essential genes encoding for example amino acid biosynthesis genes (see figure 1). Furthermore, the vector has been modified with restriction sites that are flanked by expression control sequences of for example e178 (see figure 5). However, the vector will have natural restriction sites that are found within range of natural promoters. SSV1 comprises a number of promoters for example Tind is inducible by IV irradiation (see e.g. 1401, col 1, ¶ 2). However a number of the promoters (see e.g. figure 5) are constitutive. In figure 5 is a shuttle vector that further comprises an E. coli origin of replication as well as a variant of a reporter gene and a marker.

Response to Amendment.

Applicants argue that SSV1 is an organism distinct from sulfolobus. As well, applicants argue that the vector of Stedman et al does not disclose an SSV1 expression vector with any non-viral genes let alone one or more selectable markers encoding an essential protein for Sulfolobus nor introduction thereof. However, applicants throughout the claims and the specification refer to both the virus and the cell with equivalent terms. Specifically, the claims recite for example, a sulfolobus origin of replication and in claim 2 wherein the sulfolobus origin of replication is from SSV1 or SSV2. Hence, in an embodiment embraced by the claims, each of the elements are

from SSV1 or SSV2. In other words, the origin or replication, the structural proteins, the site specific integrase and the packaging signal are all from SSV1. This leaves expression control sequences and a restriction enzyme recognition site. There is no limitation as to the source of these additional elements, hence, the elements can be from SSV1 as well. In this case, all of the vector items are plausible from SSV1.

As well, it is not clear why reference to sulfolobus in the claims can mean SSV1 or SSV2 in some instances and yet other references to sulfolobus essential proteins cannot embrace this same meaning. Applicants argue that the definition of the essential protein is to a cellular protein. However, the following definition is present in the specification. While, the sulfobulos proteins are preferred, there is no explicit definition limiting the proteins to those from the cell and not the virus.

> [0017] In yet another preferred embodiment of the invention, the selectable marker gene of the expression vector encodes an essential protein of Sulfolobus. In a more preferred embodiment of the present invention, the essential gene is a gene of the de novo nucleotide anabolism, a gene of the amino acid biosynthesis or a gene conferring antibiotic resistance. In another more preferred embodiment, the vector contains orotidine-5'-monophosphatase pyrophosphorlyase and orotidine-5'-monophosphatase decarboxylase (pyrEF) as selectable marker genes (Martusewitsch et al. 2000).

In interpreting the claims, the broadest reasonable interpretation must be used. In this case, there is no distinction in the claims or in the specification for those components that are based in the virus and those that are based in the cell. However, applicants would wish for some distinction solely based upon arguments. In other words, by reference to sulfolobus, the claims suggest that either the virus or the cell is involved. Applicants cannot pick one interpretation over the other as both interpretation s are valid when considering the full scope of the claims. Secondly, the arguments that the construct of Stedman et al does not require an introduced gene or a gene of

interest is outside of the scope of the claims which only require that the vector be capable of accepting a gene of interest. All vectors such as viral vectors are capable of carrying heterologous genes as well accepting sequence for transfer. There is no reason to believe that SSV1 cannot do so also.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 5, 6, 8-17, 21 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stedman et al Genetics **152:** 1397–1405 (August 1999) in view of Pompejus et al (6,927,026 see entire document).

Applicants claim a vector comprising (a) a sulfolobus origin of replication; (b) coding sequences for structural proteins, a coding sequence for the site-specific integrase and a packaging signal, wherein each of the structural protein coding sequences the site-specific integrase coding sequence and the packaging signal are from one of SSV1, SSV2 or pSSVx and are operably linked to expression control sequences and the packaging signal; (c) one or more selectable marker gene(s) encoding an essential protein of sulfolobus, operatively linked to sulfolobus expression control sequences; and (d) a sulfolobus promoter followed 3' by a restriction enzyme recognition site or a multiple cloning site for insertion of a gene of interest and the vector further comprises an optional 3' regulatory element

Stedman et al teach use of an antibiotic resistance marker. However, Pompejus et al teach that it is preferable that the marker

> displays high transformation efficiency, is easily selectable and makes counterselection possible

Pompejus et al teach that this system is best with a cell line deficient for the enzyme (see example 11).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the antibiotic resistance marker of Stedman et al with the orotidine-5'-decarboxylase taught by Pompejus et al because Stedman et al teach that it is within the ordinary skill of the art to include a marker in the SSV1 vector and derivatives and because Pompejus et al teach that it is within the ordinary skill of the art to use orotidine-5'-carboxylase. One would have been motivated to do so in order to receive the expected benefit of cells with high transformation efficiency with easy selection can be transformed with high yield and is easily counterselectable and which makes it possible to insert genes into microorganisms. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARIA MARVICH whose telephone number is (571)272-0774. The examiner can normally be reached on M-F (7:00-4:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, PhD can be reached on (571)-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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